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EXAMINER
STEADMAN, DAVID J

ART UNIT	PAPER NUMBER
1652	11

DATE MAILED: 12/14/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/531,266	DUNICAN ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-7 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-7 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 & 9 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 1-7 are pending in the application.

Applicants' election of Group I, claims 1-7, drawn to polynucleotides encoding a transaldolase and a host cell and cancellation of claims 8-16 in Paper No. 8, filed 10/11/01 is acknowledged.

Drawings

1. The drawings submitted with this application have not been reviewed by a draftsperson. Upon allowance of claimed subject matter, a draftsperson will perform a review. Direct any inquiries concerning drawing review to the Drawing Review Branch (703) 305-8404.

Specification/Informalities

2. The specification is objected to because of the following informalities: 1) the abstract contains more than a single paragraph; 2) there is a large blank section at pages 2 and 19; and 3) there is no "Brief Description of the Drawings" section.

3. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows: An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

If applicant desires priority under 35 U.S.C. 119(e) based upon a previously filed co-pending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph.

Claim Objections

4. Claims 1, 5, and 6 are objected to for the use of the term "SEQ ID NO.". It is suggested that the term be replaced with "SEQ ID NO:".

5. Claim 1(A)-(D) is objected to because of the following informalities: the terms "polynucleotide" in line 1 of parts (A)-(D) is grammatically incorrect and should be replaced with, for example, "a polynucleotide". Appropriate correction is required.

6. Claim 2 is objected to because of the recitation of "tkt, zwf, opcA and devB". Abbreviations, unless otherwise obvious and/or commonly used in the art, should not be recited in the claims without at least once reciting the entire phrases for which the abbreviations are used. Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

> The following is a quotation of the second paragraph of 35 U.S.C. 112:
>
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 1(C) (claims 2-5 and 7 dependent therefrom) and 6(iii) are indefinite in the recitation of "polynucleotide which is complementary" in claim 1(C) and "sequence which hybridizes with the sequences complementary to" in claim 6(iii). Neither the specification nor the claims provide a definition of the term "complementary" and it is unclear whether the complementary sequence is a partial or complete complement. It is suggested that applicants clarify their meaning of the terms by replacing the terms with, for example "polynucleotide which is completely complementary" in claim 1 and "sequence which hybridizes with the completely complementary sequences of" in claim 6(iii).

9. Claim 2 (claims 4-6 dependent therefrom) is indefinite in the recitation of "polynucleotide is a preferably recombinant DNA". A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language.

10. Claim 2 (claims 4-6 dependent therefrom) is indefinite in the recitation of "nucleotide sequences which codes for the genes tkt, zwf, opcA and devB". The specification fails to teach which identifying characteristics distinguish tkt, zwf, opcA, and devB genes. The application teaches that the tkt gene encodes a tranketolase, zwf encodes a glucose-6-phosphate dehydrogenase, and opcA and devB encode undisclosed proteins but fails to provide identifying characteristics of said genes, e.g., nucleic acid sequence. It is suggested that, for example, applicants provide identifying characteristics of said genes.

11. Claim 2 (claims 4-6 dependent therefrom) is confusing in the recitation of "A polynucleotide as claimed in claim 1 wherein the polynucleotide... ...contains at least one of the nucleotide sequences". It is unclear as to whether at least one of the tkt, zwf, opcA, and devB genes are contained in, i.e., inserted in, the polynucleotide of claim 1 or are contained in a plasmid that also contains the polynucleotide of claim 1. It is suggested that applicants clarify the meaning of the claim. The examiner has used the latter interpretation of the claim for examination.

12. Claims 4 and 6(ii) are confusing in the recitation of "one of the nucleotide sequences as shown in SEQ ID NO[:]3" in claim 4 and "at least one sequence which corresponds to sequences (i)" in claim 6(ii). It is unclear how a single nucleotide sequence can be a plurality of nucleotide sequences as the claim would suggest. It is suggested that applicants replace the terms with, for example, "the nucleotide sequence as shown in SEQ ID NO:3" in claim 4 and "the sequence of (i)" in claim 6(ii).

13. Claim 6(i) is indefinite in the recitation of "a nucleotide sequence as shown in SEQ ID NO[:]3". It is suggested that applicants replace the term with, for example, "the nucleotide sequence as shown in SEQ ID NO:3".

14. The term "corresponds to sequences (i) within the range of the degeneration of the genetic code" in claim 6(ii) is unclear and confusing. The is not defined by the claim nor the specification and the meaning of this term is unclear. It is suggested that the language term "corresponds to sequences (i) within the range of the degeneration of the genetic code" be replaced with a term that has a more clearly identifiable meaning, for example, "is a degenerate variant of SEQ ID NO:9" or "encodes the amino acid sequence of SEQ ID NO:10".

15. Claim 6(iii) is indefinite in the recitation of "hybridizes" as this term is unclear absent a statement of the conditions under which the hybridization reaction is preformed. Nucleic acids which will hybridize under some hybridization conditions will not necessarily hybridize under different conditions. It is suggested that, for example, applicants provide specific hybridization conditions in the claim.

16. Claim 6(iv) is unclear in the recitation of "sense mutations of neutral function of (i)". It is unclear from the claim as written as to the function of the nucleic acid sequence shown in SEQ ID NO:1. It is suggested that applicants clearly define their intended function of the nucleic acid of SEQ ID NO:1.

17. Claim 7 is confusing in the recitation of "a vector which carries a polynucleotide". It is suggested that the term be replaced with, for example, "a vector comprising a polynucleotide".

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 (claims 3 and 7 dependent therefrom) and 2 (claims 4-6 dependent therefrom) are directed to a genus of: a) polynucleotides that are 70 % identical to polynucleotides encoding the polypeptides of SEQ ID NOs:2 or 4, b) polynucleotides encoding polypeptides that are 70 % identical to the polypeptides of SEQ ID NOs:2 or 4, complements of a) or b), or polynucleotides having at least 15 successive bases of a), b) or c) (claim 1), and optionally wherein the polynucleotide is in a vector coding for tkt, zwf, opcA, and devB genes (claim 2). The specification does not contain any disclosure of the function of all polynucleotides that are 70 % identical to polynucleotides encoding the polypeptides of SEQ ID NOs:2 or 4, polynucleotides encoding polypeptides that are 70 % identical to the polypeptides of SEQ ID NOs:2 or 4, complements thereof, or polynucleotides comprising at least 15 successive bases of a), b), or c). The genus of nucleic acids that comprise the above described polynucleotides is a *large variable genus* with the potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species of the claimed genus, i.e., SEQ ID NO:9 which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Furthermore, the specification fails to describe any representative species of tkt, zwf, opcA, and devB genes by any identifying characteristics or properties other than being tkt, zwf, opcA, and devB genes. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

19. Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polynucleotide of SEQ ID NO:9, does not reasonably provide enablement for: a) *any* polynucleotide that is 70 % identical to a polynucleotide encoding the polypeptides of SEQ ID NOs:2 or 4, b) *any* polynucleotide encoding a polypeptide that is 70 % identical to the polypeptides of SEQ ID NOs:2 or 4, *any* complements of a) or b), or *any* polynucleotide having at least 15 successive bases of a), b) or c) (claim 1), and optionally wherein the polynucleotide is in a vector coding for *any* tkt, zwf, opcA, and devB genes (claim 2). The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1 (claims 3 and 7 dependent therefrom) and 2 (claims 4-6 dependent therefrom) are so broad as to encompass: a) *any* polynucleotide that is 70 % identical to a polynucleotide encoding the polypeptides of SEQ ID NOs:2 or 4, b) *any* polynucleotide encoding a polypeptide that is 70 % identical to the polypeptides of SEQ ID NOs:2 or 4, *any* complements of a) or b), or *any* polynucleotide having at least 15 successive bases of a), b) or c), and optionally wherein the polynucleotide is in a vector coding for *any* tkt, zwf, opcA, and devB genes. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides and tkt, zwf, opcA, and devB genes broadly encompassed by the claims. Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the polypeptide's structure relates to its function. However, in this case the disclosure is limited to polynucleotide of SEQ ID NO:9.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a polynucleotide's sequence where nucleic acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any polynucleotide and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given polynucleotide to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass: a) *any* polynucleotide that is 70 % identical to a polynucleotide encoding the polypeptides of SEQ ID NOs:2 or 4, b) *any* polynucleotide encoding a polypeptide that is 70 % identical to the polypeptides of SEQ ID NOs:2

or 4, *any* complements of a) or b), or *any* polynucleotide having at least 15 successive bases of a), b) or c), and optionally wherein the polynucleotide is in a vector coding for *any* tkt, zwf, opcA, and devB genes because the specification does not establish: (A) nucleotide sequences of *any* tkt, zwf, opcA, and devB genes or methods of isolating *any* tkt, zwf, opcA, and devB genes and said genes were not well known in the art at the time of the invention; (B) regions of the encoded protein's structure which may be modified without effecting the activity of the gene product of SEQ ID NO:9; (C) the general tolerance of the gene product of SEQ ID NO:9 to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any amino acid residues of the gene product of SEQ ID NO:9 with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including *any* polynucleotide that is 70 % identical to a polynucleotide encoding the polypeptides of SEQ ID NOs:2 or 4, *any* polynucleotide encoding a polypeptide that is 70 % identical to the polypeptides of SEQ ID NOs:2 or 4, *any* complements thereof, or *any* polynucleotide having at least 15 successive bases thereof, and optionally wherein the polynucleotide is in a vector coding for *any* tkt, zwf, opcA, and devB genes. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re* Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re* Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

20. Claims 1, 2, 6, and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by IDS reference OR (JP 09224661). Claims 1, 2, and 6 are drawn to a polynucleotide selected from: a) a polynucleotide which is at least 70 % identical to a polynucleotide encoding SEQ ID NO:2 or 4; b) a polynucleotide which encodes polypeptide that is at least 70 % identical to the polypeptide of SEQ ID NO:2 or 4; c) a polynucleotide that is complementary to a) or b); and d) a polynucleotide with at least 15 successive bases of a), b), or c) (claim 1), and optionally wherein the polynucleotide is a recombinant DNA capable of replication in Coryneform bacteria and contains at least one sequence coding for tkt, zwf, opcA and devB genes (claim 2), and optionally wherein the DNA comprises: (i) the polynucleotide of SEQ ID NO:3, (ii) a degenerate variant of SEQ ID NO:3, (iii) a sequence that hybridizes with complement of (i) or (ii), and functionally neutral sense mutations of (i), and a Coryneform bacterium comprising a vector with a polynucleotide of claim 1 (claim 7). OR teaches a zwf gene isolated from *Corynebacterium glutamicum* that encodes a glucose-6-phosphate dehydrogenase polypeptide that is 100 % identical to amino acids 253 to 299 of SEQ ID NOs:2 and 4 (see sequence comparison). OR teaches transformation of *C. glutamicum* with an expression vector comprising said zwf gene for polypeptide expression. This anticipates claims 1, 2, 6, and 7 as written.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over OR. Claim 3 is drawn to the polynucleotide of claim 1 wherein the polynucleotide is an RNA.

OR discloses the teachings as described above.

Also, one of ordinary skill in the art at the time of the invention would have recognized that the cDNA encoding the glucose-6-phosphate dehydrogenase of OR was generated from an mRNA template.

Therefore, it would have been obvious to one of ordinary skill in the art to isolate *C. glutamicum* mRNA, generate the cDNA of OR by reverse-transcriptase PCR, insert said cDNA into an expression vector, transform *C. glutamicum* with said expression vector, and express the glucose-6-phosphate dehydrogenase of OR. One would have been motivated for to isolate *C. glutamicum* mRNA, generate the cDNA of '661, insert said cDNA into an expression vector, transform *C. glutamicum* with said expression vector, and express the glucose-6-phosphate dehydrogenase of OR in order to purify and characterize *C. glutamicum* glucose-6-phosphate dehydrogenase because of the teaching of OR. One would have a reasonable expectation of success for isolating mRNA, converting the mRNA to cDNA, inserting the cDNA into an expression vector and expressing the cDNA of OR because of the knowledge of an ordinarily skilled artisan and the results of OR. Therefore, claim 3, drawn to the polynucleotide of claim 1 wherein the polynucleotide is an RNA would have been obvious to one of ordinary skill in the art.

Conclusion

22. No claim is in condition for allowance. All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The examiner can normally be reached Monday-Friday from 8:00 am to 4:30 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for this Art Unit is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600